REMARKS

Reconsideration is requested.

Claims 1-3 and 5-18 are pending. Claim 18 has been withdrawn from consideration. Claim 4 was canceled, without prejudice, in the Amendment filed February 7, 2001. Claims 1-3 and 5-17 are under active consideration.

The specification has been amended to include a new Abstract. Withdrawal of the objection to the Abstract noted in paragraph 1 of the Office Action dated February 27, 2001 (Paper No. 6) is requested.

The Section 112, second paragraph, rejection of claims 1-3, 6, 10, 15 and 16 is, to the extent not obviated by the above amendments, traversed. Reconsideration and withdrawal of the rejections are requested in view of the above and the following comments.

The applicants note the term "efficiency" is defined in the specification at page 2, lines 5-7. The Examiner's suggested amendment in paragraph 4 of Paper No. 6 has been incorporated in the above amendments. The Examiner's objection to the term "activity" would appear to also be overcome by the amendment suggested in paragraph 4 of Paper No. 6. Moreover, the applicants submit that one of ordinary skill in the art would appreciate that the stability recited in the claims is in terms of activity. Provided this is eliminated, the problems associated with undesired contaminants will be overcome. When dealing with enzymes, for example, it is not generally necessary to destroy the primary amino acid structure in order to eliminate activity but it may merely be necessary to effect the secondary or tertiary folding structure. The amended claims are submitted to be definite. Entry of the above amendment and withdrawal of the Section 112, second paragraph, rejection of claims 1-3, 6, 10, 15 and 16 are requested.

The Section 112, first paragraph, rejection of claims 1-3, 5, 6, 10 and 12-17 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

The Examiner will appreciate that the amended claims recite specific conditions which may be used to destabilize the activity and that the "undesired protein" should be one which is destructive of the end use of the protein.

U.S. Patent Application of SQUIRRELL et al
Serial No 09/529,722

Moreover, the applicants respectfully submit that, in practical terms, there is generally no need to eliminate every trace of every contaminant from a particular product. Contaminants which are of particular concern are those having a direct impact on the usefulness of the end product, as set out at the bottom of page 2 of the specification. Such contaminants are recognized by those of ordinary skill in the art who are also aware of the types of activity which cause problems with a particular end product and therefore are the focus of one of ordinary skill in the art. That is, once the activity has been identified, it would be a matter of routine experimentation to find mutants where the stability of the proteins, such as enzymes, under desired conditions, such as temperature or pH, were decreased. For example, random mutagenesis of the proteins will produce a range of clones which may be subjected to, for example, elevated temperature, and then retested for activity. Those enzymes which lost activity under these conditions might then be used in the method of the present invention. Such experimentation is routine and not undue as mutagenesis and library screening are well known to those of ordinary skill in the art. Finally, it would be a matter of routine experimentation to confirm that target peptide products were not disrupted under these conditions.

As an illustration of the presently claimed invention, the applicants have performed the following series of experiments demonstrating the heat denaturation of two different restriction enzymes in the presence of thermostable restriction enzymes. Specifically, restriction digests were performed on pUC19 plasmid DNA using both untreated restriction enzymes and restriction enzymes that had been treated to 65°C for 20 minutes. Digests were carried out using the methods described in Sambrook et al (1989), as will be known to those of ordinary skill in the art. Gel electrophoresis was carried out using a 0.9% agarose gel stained with ethidium bromide.

The wells of the gel are shown as follows:

1. pUC19 DNA with no restriction enzymes (control)
2. Untreated KpnI with pUC19
3. Heat-treated KpnI with pUC19
4. Untreated AatII with pUC19
5. Heat-treated AatII with pUC19
6. Untreated SspI with pUC19
7. Heat-treated SspI with pUC19

8. Untreated KpnI/AatII with pUC19

9. Heat-treated KpnI/SspI with pUC19

10. Untreated KpnI/SspI with pUC19

11. Heat-treated KpnI/SspI with pUC19

12. Untreated KpnI/SspI/AatII with pUC19

13. Heat-treated KpnI/SspI/AatII with pUC19

The results of this experiment are shown in the attached photograph wherein it can be seen that all cases where AatII and SspI were heat-treated, they were unable to cut the pUC19 DNA, while KpnI was able to function normally. This was shown in the wells where heat-treated AatII and SspI were used (without KpnI), the pattern of bands was the same as the control, uncut DNA. In wells where mixtures of untreated restriction enzymes were used, two bands of smaller size were present. The bands in wells 9, 11 and 13, where there were mixtures of heat-treated restriction enzymes, only one band was present. This suggests that only one of the enzymes was functioning correctly, and the results shown in wells 3, 5 and 7 indicate that this was KpnI.

The applicants respectfully submit the above illustration of the presently claimed invention demonstrates, for example, that a reasonable amount of experimentation may be required to allow differentiation on the basis of heat stability. Similar experiments may be conducted with any desired protein whose activity is hindered by an unwanted protein.

Withdrawal of the Section 112, first paragraph, rejection of claims 1-3, 5, 6, 10 and 12-17 is requested.

In view of the above, the claims are submitted to be in condition for allowance and a Notice to that effect is requested.

U.S. Patent Application of SQUIRRELL et al
Serial No.: 09/529,722

Respectfully submitted,

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U.S. Patent Application of ***SQUIRRELL*** *et al*
Serial No.: 09/529,722

MARKED-UP COPY OF AMENDED CLAIMS WHEREIN STRIKEOUTS ARE TO BE DELETED AND UNDERLINED IS TO BE ADDED

1. (Twice Amended) A method for producing a polypeptide product which is substantially free of an undesired protein wherein the undesired protein has activity that ~~which is a protein whose activity~~ is essential for survival ~~or efficiency~~ of a host cell or for a viable production process using the host cell, and has activity that hinders the use of the polypeptide product, the process comprising culturing a host cell which is able to express said polypeptide product and which is able to express said undesired protein only in a mutant form which form has the said activity of the corresponding native protein under culture conditions but loses said activity ~~is unstable~~ under conditions of pH or temperature at which the said polypeptide product remains unaffected~~stable~~; and recovering the desired product, wherein either the host cell culture or the recovered product is subjected for a sufficient period of time to conditions of pH or temperature under which the undesired protein is ~~unstable so as to~~ denatured ~~the undesired protein~~ but the polypeptide product remains unaffected.

2. (Amended) A method according to claim 1 wherein the host cells are cultured for a period which is sufficient to allow production of polypeptide product, and then a batch of said culture is subjected to the said conditions of pH or temperature under which the undesired protein is ~~unstable for a sufficient period of time to~~ denatured ~~the undesired protein~~, and the polypeptide product is recovered.

5. (Three Times Amended) A method according to claim 1 or claim 2 wherein the conditions at which the undesired protein is denatured and the polypeptide product remains ~~stable~~ unaffected are temperature conditions.

6. (Three Times Amended) A method according to claim 1 or claim 2 wherein the conditions at which the undesired protein is denatured and the polypeptide product remains ~~stable~~ unaffected are pH conditions.

10. (Twice Amended) A recombinant cell which comprises a first nucleotide sequence which encodes a desired polypeptide under the control of regulatory elements which allow expression of said polypeptide, and wherein a gene which encodes a protein which is undesirable as a contaminant in preparations of said polypeptide product but wherein the undesired protein has activity that is essential for survival of a host cell or for a viable production process using the host cell and has activity which impedes or hinders the use of the polypeptide product ~~whose activity is essential for survival or efficiency of a host cell~~, is mutated such that the protein expressed is denatured~~unstable~~ under pH or temperature conditions in which the polypeptide product remains unaffected~~stable~~.